Ultragenyx and Mereo BioPharma Announce Interim Phase 2 Data from Phase 2/3 Orbit Study Demonstrating Setrusumab (UX143) Significantly Reduced Fracture Rates in Patients with Osteogenesis Imperfecta (OI)

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Phase 2 data presented at ASBMR 2023 show treatment with setrusumab resulted in 67% reduction in annualized fracture rate associated with continuous and meaningful improvements in bone mineral density (BMD)

Ultragenyx hosting Analyst Day on Monday, October 16 at 8:30 a.m. ET

NOVATO, Calif., VANCOUVER, British Columbia and LONDON, Oct. 14, 2023 (GLOBE NEWSWIRE) -- Ultragenyx Pharmaceutical Inc. (NASDAQ: RARE) and Mereo BioPharma Group plc (NASDAQ: MREO) today announced interim data from the Phase 2 portion of the Phase 2/3 *Orbit* study demonstrating that treatment with setrusumab (UX143) significantly reduced incidence of fractures in patients with OI with at least 6 months of follow-up and continues to demonstrate ongoing and meaningful improvements in lumbar spine bone mineral density (BMD). The data were presented in a late-breaker presentation at the American Society for Bone and Mineral Research 2023 Annual Meeting (ASBMR).

As of the cut-off date and following at least 6 months of treatment with setrusumab, the annualized fracture rate across all 24 patients in the Phase 2 portion of the study was reduced by 67%. In the 2 years prior to treatment with setrusumab all patients experienced at least 1 fracture. The median annualized fracture rate of 0.72 in the 2 years prior to treatment was reduced to 0.00 (n=24, p=0.042) during the mean treatment duration period of 9 months. Following initiation of treatment with setrusumab, 20 patients experienced no radiographic-confirmed fractures, and 4 patients experienced 7 radiographic-confirmed fractures in 5 separate events. These fractures exclude fractures of the fingers, toes, skull, and face consistent with the Phase 3 study design.

“I have not yet encountered a patient with a fragility fracture while on setrusumab, and this may result from setrusumab’s effects on the skeleton, improving the rate of new bone formation and bone quality,” said Gary Gottesman, M.D., Professor of Pediatrics and Medicine, Washington University School of Medicine. “Some of the kids feel well enough they are participating in activities that they might normally avoid and have suffered some relatively minor fractures.”

The reduction in annualized fracture rates was associated with a clinically meaningful increase in BMD. At the 6-month timepoint, treatment with setrusumab resulted in a mean increase in lumbar spine BMD from baseline of 13% at 20 mg/kg (n=11) and 16% at 40 mg/kg (n=8), which represents the same substantial mean improvement in Z-score of +0.85 for both dose groups at 6 months compared to a combined mean baseline Z-score of –1.68. The small apparent difference in BMD change from baseline is likely related to differences in patients assigned to the two treated groups. There was no statistically significant difference in BMD percent change or Z-score change from baseline between the 20 and 40 mg/kg dosing cohorts.

“These data provide compelling evidence that improved bone mineral density, resulting from this unique mechanism of action, reduced the risk of fractures and that treatment with setrusumab could allow patients with OI to lead much more active lives with fewer fractures,” said Eric Crombez, M.D., chief medical officer at Ultragenyx. “I want to acknowledge the OI community and especially thank the people living with OI and their caregivers who have aided the setrusumab development program so that we may potentially offer the first approved treatment option for this severe and disabling disease.”

As of the data cut-off, there were no treatment-related serious adverse events observed in the study. Reported adverse events were generally consistent with those observed in the *ASTEROID* study with infusion-related events and headache determined to be the most common adverse events related to the study drug. There have been no reported hypersensitivity reactions related to setrusumab. There were no notable safety-related differences observed between dosing groups or age groups.

The Phase 3 portion of the study is currently enrolling approximately 195 patients at 50 sites across 12 countries.

U.S. residents can learn more by visiting ultraclinicaltrials.com.

Analyst Day and Webcast Information

Ultragenyx will host an Analyst Day at 8:30 a.m. ET on Monday, October 16, 2023 to discuss these data and to provide an update on the company’s development pipeline. A live video webcast of the program will be available at https://www.webcaster4.com/Webcast/Page/359/49192.
An archived version of the remarks will also be available through the Ultragenyx website.

The Setrusumab Phase 3 Program

The global, seamless Phase 2/3 Orbit study is evaluating the effect of setrusumab on clinical fracture rate in patients aged 5 to <26 years. In the Phase 2 portion, 24 patients were randomized 1:1 to receive setrusumab at one of two doses to determine the optimal dosing strategy for Phase 3. The pivotal Phase 3 portion of the study will include approximately 195 patients at 50 sites across 12 countries, randomized 2:1 to receive setrusumab or placebo, with a primary efficacy endpoint of annualized clinical fracture rate, excluding fingers, toes, skull, and face. All patients will transition to an extension period and receive open-label setrusumab after the Phase 3 primary analysis is complete.

The global Phase 3 Cosmic study is an open-label, randomized, active-controlled study in patients aged 2 to <7 years evaluating setrusumab compared to intravenous bisphosphonates (IV-BP) therapy on reduction in total fracture rate, including morphometric vertebral fractures. The Cosmic study will enroll approximately 65 patients at more than 20 sites across 8 countries.

About Osteogenesis Imperfecta (OI)

Osteogenesis Imperfecta (OI) includes a group of genetic disorders impacting bone metabolism. Approximately 85% to 90% of OI cases are caused by mutations in the *COL1A1 or COL1A2* genes, leading to either reduced or abnormal collagen and changes in bone metabolism. The collagen

mutations in OI can result in increased bone brittleness, which contributes to a high rate of fractures. Patients with OI also exhibit inadequate production of new bone, which leads to decreased bone mass, bone fragility and weakness. OI can also lead to bone deformities, abnormal spine curvature, pain, decreased mobility, and short stature. No treatments are approved for OI, which affects approximately 60,000 people in the developed world.

About Setrusumab (UX143)

Setrusumab is a fully human monoclonal antibody that inhibits sclerostin, a negative regulator of bone formation. Blocking sclerostin is expected to increase new bone formation, bone mineral density and bone strength in OI. In mouse models of OI, the use of anti-sclerostin antibodies was shown to increase bone formation, improve bone mass to normal levels, and increase bone strength against fracture force testing to normal levels.

In 2019 Mereo BioPharma completed the Phase 2b dose-finding study (*ASTEROID*) for setrusumab in 112 adults with OI. The *ASTEROID* study demonstrated treatment with setrusumab resulted in a clear, dose-dependent and statistically significant effect on bone formation and bone density at multiple anatomical sites among adult participants with OI.

Ultragenyx and Mereo BioPharma are collaborating on the development of setrusumab globally based on the collaboration and license agreement between the parties. The companies have developed a comprehensive late-stage program to continue development of setrusumab in pediatric and young adult patients across OI sub-types I, III and IV.

About Ultragenyx

Ultragenyx is a biopharmaceutical company committed to bringing novel products to patients for the treatment of serious rare and ultra-rare genetic diseases. The company has built a diverse portfolio of approved therapies and product candidates aimed at addressing diseases with high unmet medical need and clear biology for treatment, for which there are typically no approved therapies treating the underlying disease.

The company is led by a management team experienced in the development and commercialization of rare disease therapeutics. Ultragenyx's strategy is predicated upon time- and cost-efficient drug development, with the goal of delivering safe and effective therapies to patients with the utmost urgency. For more information on Ultragenyx, please visit ultragenyx.com.

About Mereo BioPharma

Mereo BioPharma is a biopharmaceutical company focused on the development of innovative therapeutics for rare diseases. The Company has two rare disease product candidates, setrusumab for the treatment of Osteogenesis Imperfecta (OI) and alvelestat primarily for the treatment of severe alpha-1-antitrypsin deficiency-associated lung disease (AATD-LD). The Company's partner, Ultragenyx Pharmaceutical, Inc., has initiated a pivotal Phase 2/3 pediatric study in young adults (5 to <26 years old) for setrusumab in OI and a Phase 3 study in pediatric patients (2 to <7 years old) in the first half of 2023. The partnership with Ultragenyx includes potential milestone payments of up to $245 million (following the recent $9 million milestone) and royalties to Mereo on commercial sales in Ultragenyx territories. Mereo has retained EU and UK commercial rights and will pay Ultragenyx royalties on commercial sales in those territories. Setrusumab has received orphan designation for osteogenesis imperfecta from the EMA and FDA, PRIME designation from the EMA and has pediatric disease designation from the FDA. Alvelestat has received U.S. Orphan Drug Designation for the treatment of AATD, Fast Track designation from the FDA, and positive data were reported from a Phase 2 proof-of-concept study in North America, Europe and the UK. In addition to the rare disease programs, Mereo has two oncology product candidates in clinical development. Etigilimab (anti-TIGIT) has completed enrollment in a Phase 1b/2 basket study evaluating its safety and efficacy in combination with an anti-PD-1 in a range of tumor types including three rare tumors and three gynecological carcinomas - cervical, ovarian, and endometrial and is in an ongoing Phase 1b/2 investigator led study at the MD Anderson Cancer Center in clear cell ovarian cancer; navicixizumab, for the treatment of late line ovarian cancer, has completed a Phase 1 study and has been partnered with OncXerna Therapeutics, Inc. in a global licensing agreement that includes payments of up to $300 million in milestones and royalties.

For more information on Mereo BioPharma, please visit www.mereobiopharma.com.

Ultragenyx Forward-Looking Statements and Use of Digital Media

Except for the historical information contained herein, the matters set forth in this press release, including statements related to Ultragenyx's expectations and projections regarding its future operating results and financial performance, business plans and objectives for UX143, expectations regarding the tolerability and safety of UX143, and future clinical and regulatory developments for UX143 are forward-looking statements within the meaning of the "safe harbor" provisions of the Private Securities Litigation Reform Act of 1995. Such forward-looking statements involve substantial risks and uncertainties that could cause our clinical development programs, collaboration with third parties, future results, performance or achievements to differ significantly from those expressed or implied by the forward-looking statements. Such risks and uncertainties include, among others, the uncertainty of clinical drug development and unpredictability and lengthy process for obtaining regulatory approvals, the ability of the company and Mereo BioPharma to successfully develop UX143, the company's ability to achieve its projected development goals in its expected timeframes, risks related to adverse side effects, risks related to reliance on third party partners to conduct certain activities on the company's behalf, the potential for any license or collaboration agreement, including the company's collaboration agreement with Mereo to be terminated, smaller than anticipated market opportunities for the company's products and product candidates, manufacturing risks, competition from other therapies or products, and other matters that could affect sufficiency of existing cash, cash equivalents and short-term investments to fund operations, the company's future operating results and financial performance, the timing of clinical trial activities and reporting results from same, and the availability or commercial potential of Ultragenyx's products and drug candidates. Ultragenyx undertakes no obligation to update or revise any forward-looking statements. For a further description of the risks and uncertainties that could cause actual results to differ from those expressed in these forward-looking statements, as well as risks relating to the business of Ultragenyx in general, see Ultragenyx's Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission (SEC) on August 4, 2023, and its subsequent periodic reports filed with the SEC.

In addition to its SEC filings, press releases and public conference calls, Ultragenyx uses its investor relations website and social media outlets to publish important information about the company, including information that may be deemed material to investors, and to comply with its disclosure obligations under Regulation FD. Financial and other information about Ultragenyx is routinely posted and is accessible on Ultragenyx's Investor Relations website (https://ir.ultragenyx.com/) and LinkedIn website (https://www.linkedin.com/company/ultragenyx-pharmaceutical-inc-/).

Mereo BioPharma Forward-Looking Statements

This press release contains "forward-looking statements." All statements other than statements of historical fact contained in this press release are forward-looking statements within the meaning of Section 27A of the United States Securities Act of 1933, as amended (the "Securities Act"), and Section 21E of the United States Securities Exchange Act of 1934, as amended (the "Exchange Act"). Forward-looking statements usually relate to future events and anticipated revenues, earnings, cash flows or other aspects of Mereo BioPharma's operations or operating results. Forward-looking statements are often identified by the words "believe," "expect," "anticipate," "plan," "intend," "foresee," "should," "would," "could," "may," "estimate," "outlook" and similar expressions, including the negative thereof. The absence of these words, however, does not mean that the statements are not

forward-looking. These forward-looking statements are based on Mereo BioPharma's current expectations, beliefs and assumptions concerning future developments and business conditions and their potential effect on Mereo. While management believes that these forward-looking statements are reasonable as and when made, there can be no assurance that future developments affecting Mereo BioPharma will be those that it anticipates.

All of Mereo BioPharma's forward-looking statements involve known and unknown risks and uncertainties some of which are significant or beyond its control and assumptions that could cause actual results to differ materially from Mereo BioPharma's historical experience and its present expectations or projections.

Such risks and uncertainties include, among others, the uncertainties inherent in the clinical development process; Mereo BioPharma's reliance on third parties to conduct and provide funding for its clinical trials; Mereo's dependence on enrollment of patients in its clinical trials; and Mereo's dependence on its key executives. You should carefully consider the foregoing factors and the other risks and uncertainties that affect Mereo BioPharma's business, including those described in the "Risk Factors" section of its latest Annual Report on Form 20-F, reports on Form 6-K and other documents furnished or filed from time to time by Mereo BioPharma with the Securities and Exchange Commission. Mereo BioPharma wishes to caution you not to place undue reliance on any forward-looking statements, which speak only as of the date hereof. Mereo BioPharma undertakes no obligation to publicly update or revise any of our forward-looking statements after the date they are made, whether as a result of new information, future events or otherwise, except to the extent required by law.

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